View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

institution. The in-hospital and short-term (up to 4 years) results have been excellent; all patients are alive and well, there has been no reoperation, and only 1 patient has residual aortic regurgitation that has been graded as mild at repeated echocardiographic examinations.

In conclusion, we share the conviction of Gerosa and colleagues that selective replacement of the dilated noncoronary sinus in association with replacement of the ascending aorta may be an excellent surgical option in patients with a well-functioning bicuspid aortic valve. We believe that the re-creation of sinuses and the remodeling of the sinotubular junction, by reducing the leaflet stress, may help to improve the long-term results of this approach.

Alfredo Giuseppe Cerillo, MD
Pier Andrea Farneti, MD
Mattia Glauber, MD
Operative Unit of Cardiac Surgery
"G. Pasquinucci" Hospital
The Institute of Clinical Physiology
The National Research Council
Massa, Italy

References

1. Gerosa G, Pontarollo S, Liceto S, Di Marco F. An alternative technique for aortic root remodeling in patients with bicuspid aortic valve. *J Thorac Cardiovasc Surg.* 2007; 133:249-50.
2. De Paulis R, De Matteis GM, Nardi P, Scaffa R, Colella DF, Chiariello L. A new aortic Dacron conduit for surgical treatment of aortic root pathology. *Ital Heart J.* 2000;1:457-63.
3. Grande-Allen KJ, Cochran RP, Reinhall PG, Kunzelmann KS. Recreation of sinuses is important for sparing the aortic valve: a finite element study. *J Thorac Cardiovasc Surg.* 2000;119:753-63.
4. De Paulis R, De Matteis GM, Nardi P, Scaffa R, Bassano C, Chiariello L. Analysis of valve motion after the reimplantation type of valve-sparing procedure (David I) with a new aortic root conduit. *Ann Thorac Surg.*. 2002l;74: 53–7.

doi:10.1016/j.jtcvs.2007.03.058

Reply to the Editor:

We read with interest the letter by Cerillo, Farneti, and Glauber, who propose a technique resembling our approach[1] for reconstruction of the ascending aorta in patients with normofunctioning bicuspid aortic valve (BAV).

The choice by Cerillo and colleagues to reconstruct the aortic root and the noncoronary sinus with a hand-crafted Valsalva sinus graft composed of two separate segments of a Dacron prosthesis, perpendicularly oriented so as to mimic the conformation of the Gelweave Valsalva graft (Sulzer Vascutek, Renfrewshire, Scotland), is a smart idea, nevertheless recalling the custom-made Valsalva graft previously proposed by Robicsek and Thubrikar.[2]

The aim is to replace the native dilated noncoronary sinus with a self-expanding neosinus, favoring a more physiologic leaflet closure with reduced stress, ultimately resulting in long-lasting preservation of native valve function.

The technique suggested by Cerillo and colleagues requires an additional suture between the two Dacron segments (graft-to-graft suture), which, in their experience, was not associated with hemorrhagic complications. However, the complexity of surgery is undoubtedly increased and the potential advantage of recreating an expandable neosinus in the presence of a BAV, which intrinsically has an impaired hydrodynamic performance, has not been demonstrated yet. It is reasonable to hypothesize that the physiologic characteristics of the aortic root differ in the presence of a bicuspid compared with those in the presence of a tricuspid valve. In his theory for aortic valve closure, Bellhouse[3] evidenced the paramount importance of the role of the sinuses, but also underlined that, in presence of a stenotic valve, the turbulent jet generated by the blood flow deceleration in end-systole is not captured by the sinuses, and no blood vortices can be evidenced in the sinuses either. More recently, Robicsek and colleagues[4] investigated specifically the blood flow pattern through the BAV by a computer-assisted digitalized model, evidencing asymmetric and stenotic abnormalities even in normally functioning valves. These abnormalities are likely to create recirculation vortices, which cannot be confined into the sinuses, like in the trileaflet valve, but extend into the ascending aorta.

Nevertheless, the data reported by Cerillo, Farneti, and Glauber strengthen the favorable results of our experience, reinforcing our conviction about the opportunity to selectively replace the ascending aorta and noncoronary sinus in patients with BAV.

Francesca di Marco, MD, PhD[a]
Sara Pontarollo, MD[b]
Sabino Illiceto, MD[b]
Gino Gerosa, MD[a]
Division of Cardiac Surgery[a]
Division of Cardiology[b]
Department of Cardiological, Thoracic and Vascular Sciences
Padua University Medical School
Padua, Italy

References

1. Gerosa G, Pontarollo S, Iliceto S, di Marco F. An alternative technique for aortic root remodeling in patients with bicuspid aortic valve. *J Thorac Cardiovasc Surg.* 2007;133: 249-50.
2. Robicsek F, Thubrikar MJ. Compliance of aortic root conduit [letter reply]. *Ann Thorac Surg.* 2003;75:2007.
3. Bellhouse BJ. Fluid mechanics of model aortic and mitral valves. *Proc R Soc Med.* 1970; 63:996.
4. Robicsek F, Thubrikar MJ, Cook JW, Fowler RT. The congenitally bicuspid aortic valve: how does it function? Why does it fail? *Ann Thorac Surg.* 2004;77:177-85.

doi:10.1016/j.jtcvs.2007.04.057

Rescue versus regeneration

To the Editor:

We read with interest the article by Suzuki and colleagues,[1] in which they examined the effects of mechanical unloading on self-regeneration of the injured heart. The model they used is a very good example of how classic surgical techniques can help answer current basic research questions. There is no doubt as to the validity of the main finding, namely, that taking the hemodynamic load off an acutely ischemic and failing heart is beneficial. We[2] have followed this strategy in the clinical setting for some time now. The one problem that we see in the authors' conclusion is perhaps merely semantic, but still deserves consideration. Throughout the article, regeneration processes are discussed that are believed to involve intrinsic stem cells, stem cell migration from the periphery or mitotic cardiomyocyte replication. However, we believe that it is very important to distinguish between the biology of myocardial rescue and that of "true" regeneration. This may be difficult based on the data from Suzuki and colleagues' article, because they unloaded the hearts as early as 1 hour after the onset of infarction. Among many other things, removing the work load markedly reduces oxygen consumption of

the myocardium (reflected, for instance, by a downregulation of respiratory chain enzymes),[3] with obvious beneficial effects on cell survival. These effects are probably most pronounced in the mechanically and biologically overburdened infarct border zone. Therefore, it does not seem surprising that the authors found less apoptosis and more markers of vital cells—including c-kit– and Sca-1–expressing cells—right there. To study true regeneration processes, however, unloading of the hearts later after myocardial infarction might produce more meaningful data. Here, the effects of myocardial rescue by unloading have abated, enabling the researcher to concentrate on true regeneration processes instead of salvage of pre-existing cells. We expect that the differences in regenerative capacity between unloaded and loaded hearts would then be much smaller, similar to the clinical observation that weaning from left ventricular assist device support during acute infarction or in nonischemic cardiomyopathy is sometimes possible,[4] but very rarely in patients with chronic ischemic heart failure.

Taken together, the data presented by Suzuki and colleagues add nicely to the evidence supporting the concept of rapid hemodynamic load reduction in acute infarction. Whether unloading alone is able to also initiate true myocardial regeneration, especially in the clinical setting, remains to be seen.

Christof Stamm, MD
Boris Nasseri, MD
Roland Hetzer, MD
Deutsches Herzzentrum Berlin
Cardiothoracic and Vascular Surgery
Berlin, Germany

References

1. Suzuki R, Li TS, Mikamo A, Takahashi M, Ohshima M, Kubo M, et al. The reduction of hemodynamic loading assists self-regeneration of the injured heart by increasing cell proliferation, inhibiting cell apoptosis, and inducing stem-cell recruitment. *J Thorac Cardiovasc Surg.* 2007;133:1051-8.
2. Potapov EV, Weng Y, Hausmann H, Kopitz M, Pasic M, Hetzer R. New approach in treatment of acute cardiogenic shock requiring mechanical circulatory support. *Ann Thorac Surg.* 2003;76:2112-4.
3. Bugger H, Leippert S, Blum D, Kahle P, Barleon B, Marme D, et al. Subtractive hybridization for differential gene expression in mechanically unloaded rat heart. *Am J Physiol Heart Circ Physiol.* 2006;291: H2714-22.
4. Dandel M, Weng Y, Siniawski H, Potapov E, Lehmkuhl HB, Hetzer R. Long-term results in patients with idiopathic dilated cardiomyopathy after weaning from left ventricular assist devices. *Circulation.* 2005;112(9 Suppl): I37-45.

doi:10.1016/j.jtcvs.2007.05.065

Reply to the Editor:

We greatly appreciate the letter from Stamm and colleagues with its well-directed comments on our article. As they suggest, we need to clarify many problems about hemodynamic unloading for myocardial repair, including "regeneration versus rescue," "acute versus chronic," and "clinical patient versus experimental model."

First, rescue and regeneration are very different biologic processes. The former involves time-limited work to rescue the surviving myocardium soon after damage, whereas the latter is a slow and long-term process of regenerating new myocardium for repairing the injured heart. We recognize that the regenerative potency of the injured heart is poor because of the very limited proliferating potency of cardiomyocytes.[1] Inasmuch as we removed hemodynamic loading soon after infarction in this study, it is possible that hemodynamic unloading rescued much of the surviving myocardium within the injured heart and contributed to the dramatic improvement in the infarcted area and the left ventricular wall thickness, as shown in Figure 1 of our article.[2] However, the increased number of Ki-67–positive cells indicated an accelerated biologic process of regeneration in the unloading infarcted heart. Furthermore, although we did not follow their fate, the increased number of stem cells in the unloading infarcted heart also played a role in myocardial repair. On the basis of this evidence, we concluded that the reduced hemodynamic loading assists self-regeneration of the injured heart.

Second, compared with the acute phase, the chronically injured heart was characterized by compensatory hypertrophy of the surviving myocardium, the senescence of cardiac stem cells,[3] and many other neurohormonal changes. Thus, it is worth investigating whether hemodynamic unloading would assist the regeneration of a chronically injured heart and the capacity and speed of this regeneration.

The final problem relates to the self-regenerative capacity of the injured heart in both patients and experimental animals. In contrast to healthy young animals, many of the patients with heart failure were older and had coexisting systemic diseases, such as diabetes, hyperlipidemia, and hypertension, which contributed to the senescence of stem cells. Naturally, the proliferating potency of cardiomyocytes and the number of cardiac stem cells in older patients with heart failure would be much weaker than those in healthy young animals.[4]

In all, the functional recovery of the failing heart achieved by left ventricular assist device support involves complex mechanisms, which will be affected by many factors.[5] Although our experimental data suggest that hemodynamic unloading assists self-regeneration of the injured heart, further study is warranted to estimate the functional contribution of myocardial regeneration in patients subjected to left ventricular assist device support.

Tao-Sheng Li, MD
Ryo Suzuki, MD
Kimikazu Hamano, MD
Department of Surgery and Clinical Science
Yamaguchi University
Graduate School of Medicine
Ube, Yamaguchi, Japan

References

1. Beltrami AP, Urbanek K, Kajstura J, Yan SM, Finato N, Bussani R, et al. Evidence that human cardiac myocytes divide after myocardial infarction. *N Engl J Med.* 2001;344: 1750-7.
2. Suzuki R, Li TS, Mikamo A, Takahashi M, Ohshima M, Kubo M, et al. The reduction of hemodynamic loading assists self-regeneration of the injured heart by increasing cell proliferation, inhibiting cell apoptosis, and inducing stem-cell recruitment. *J Thorac Cardiovasc Surg.* 2007;133:1051-8.
3. Urbanek K, Torella D, Sheikh F, De Angelis A, Nurzynska D, Silvestri F, et al. Myocardial regeneration by activation of multipotent cardiac stem cells in ischemic heart failure. *Proc Natl Acad Sci U S A.* 2005;102:8692-7.
4. von Harsdorf R, Poole-Wilson PA, Dietz R. Regenerative capacity of the myocardium: implications for treatment of heart failure. *Lancet*. 2004;363:1306-13.
5. Wohlschlaeger J, Schmitz KJ, Schmid C, Schmid KW, Keul P, Takeda A, et al. Reverse remodeling following insertion of left ventricular assist devices (LVAD): a review of the morphological and molecular changes. *Cardiovasc Res.* 2005;68:376-86.

doi:10.1016/j.jtcvs.2007.06.030